SUPPORTING INFORMATION

Supplement to: *Agreement between local and central reading of endoscopic disease activity in ulcerative colitis: results from the tofacitinib OCTAVE trials*

This appendix has been provided by the authors to give readers additional information about their work.

Supplementary appendix

1. Permitted concomitant and prohibited concomitant medications in the OCTAVE clinical programme

Patients were permitted concomitant treatment with oral 5-aminosalicylates (5-ASA) or sulfasalazine (providing the dose was not changed), and oral corticosteroids (up to 25 mg/day prednisone or equivalent; stable dose for ≥2 weeks prior to baseline of OCTAVE Induction 1 or 2); corticosteroid tapering was mandatory from baseline of OCTAVE Sustain.

1.1. Concomitant medications

OCTAVE Induction 1 and 2

The following treatments for ulcerative colitis (UC) were allowed providing they were stable for the specified period of time prior to the first dose of study medication and were not permitted to change (dose reduction or increase) during the study treatment period:

- Oral 5-ASA or sulfasalazine were allowed providing the dose was stable for at least 4 weeks prior to baseline
- Chronic treatment for UC with antibiotics (e.g. metronidazole, rifaximin) was allowed, providing that the dose was stable for at least 2 weeks prior to baseline
- Oral corticosteroids were allowed during the study up to 25 mg/day oral prednisone or equivalent, and up to 9 mg/day budesonide, providing that the dose was stable within 2 weeks of baseline. Note: for subjects that were taking >20 mg/day oral corticosteroids, the dose could have been decreased down to 20 mg/day at the investigator's discretion starting at Week 4/visit 4 and stayed at this reduced dose thereafter for the remainder of the induction study, provided their partial Mayo score

was ≤2, with no individual subscore >1 and they had a rectal bleeding subscore of 0 at Week 4. If the subject subsequently experienced signs or symptoms of worsening of UC, in the opinion of the investigator, due to the reduction in corticosteroid daily dose, the daily corticosteroid dosage for the subject could have been reverted to the preceding daily dosage instructed by the investigator; however, in those cases, no further dose decrease was allowed for the remainder of the induction study.

OCTAVE Sustain

The following treatments for UC were allowed providing their doses were not changed (dose reduction or increase), with the exception of oral corticosteroids (see below) during the study treatment period:

- Oral 5-ASA or sulfasalazine
- Chronic treatment for UC with antibiotics (e.g. metronidazole, rifaximin)
- Oral corticosteroids were allowed during the study. Since the subjects were transferred from OCTAVE Induction 1 and 2, the maximum corticosteroid dose was 25 mg/day oral prednisone or equivalent, and 9 mg/day budesonide. Tapering corticosteroids was mandatory starting the first week of the study.

OCTAVE Open

The following treatments for UC were allowed providing their doses were not changed (reduced or increased), with the exception of oral 5-ASA or sulfasalazine and oral corticosteroids (see below) during the study treatment period:

- Oral 5-ASA or sulfasalazine dose modifications during the study were permitted

- Chronic treatment for UC with antibiotics (e.g. metronidazole, rifaximin) if continued from the preceding study
- Oral corticosteroids were allowed for subjects entering OCTAVE Open on oral corticosteroids (maximum dose of 25 mg/day oral prednisone or equivalent), and tapering was required to commence starting the first week of the study
- The daily dose of oral prednisone or equivalent was decreased at a rate of 5 mg/week until the dose reached 20 mg/day, then reduced by 2.5 mg to 5.0 mg weekly until the dose reached 0 mg.

1.2. Prohibited concomitant medications

<u>OCTAVE Induction 1 and 2, OCTAVE Sustain and OCTAVE Open</u>

The following medications were prohibited:

- Azathioprine, 6-mercaptopurine, and methotrexate
- Cyclosporine, mycophenolate mofetil/mycophenolic acid, and tacrolimus
- Interferon
- Tumour necrosis factor (TNF) antagonists (e.g. infliximab, adalimumab, or certolizumab)
- Intravenous corticosteroids
- Rectally administered formulation of corticosteroids or 5-ASA
- Natalizumab, vedolizumab (specified in the OCTAVE Open protocol), or other anti-adhesion molecule therapy (including investigational agents)
- Other investigational or marketed immunosuppressants or biologics with immunomodulatory properties

- Leukocyte apheresis, including selective lymphocyte, monocyte, or granulocyte apheresis (e.g. Cellsorba®) or plasma exchange
- Moderate to potent CYP3A inducers or inhibitors due to potential for drug interactions or confounding of data interpretation
- Antimotility agents for control of diarrhoea (i.e. diphenoxylate hydrochloride with atropine sulphate or loperamide) (not prohibited in OCTAVE Open).

2. Summary of study design

Patients in OCTAVE Induction 1 and 2 received tofacitinib 10 mg twice daily (b.d.) or placebo, with final efficacy assessment at Week 8 (Figure 1). Patients who achieved clinical response (a decrease from induction study baseline total Mayo score of ≥3 points and ≥30%, plus a decrease in rectal bleeding subscore of ≥1 point or an absolute rectal bleeding subscore of 0 or 1; centrally read) in OCTAVE Induction 1 and 2 were eligible to enter OCTAVE Sustain. In OCTAVE Sustain, patients received placebo, tofacitinib 5 mg b.d., or tofacitinib 10 mg b.d., with final efficacy assessment at Week 52 (Figure 1).

OCTAVE Open included induction non-responders from OCTAVE Induction 1 and 2 and completers or treatment failures from OCTAVE Sustain (Figure 1); patients in remission at Week 52 of OCTAVE Sustain (centrally read) received tofacitinib 5 mg b.d.; all others received tofacitinib 10 mg b.d. All patients underwent endoscopy at Month 2 of OCTAVE Open; induction non-responders without clinical response at Month 2 (centrally read) were withdrawn.

3. Assessment of Mayo endoscopic subscore (MES)

For central reading, a single read was performed by a reader who was unaware of treatment assignment, study, visit and the patient's clinical status. For local reading, sites were trained

on the scoring of the MES, and methods for optimising the quality of the video recordings. Per protocol, MES was scored as: normal or inactive disease = 0; mild disease (erythema, decreased vascular pattern) = 1; moderate disease (marked erythema, absent vascular pattern, any friability, erosions) = 2; or severe disease (spontaneous bleeding, ulceration) = 3. Of note, the inclusion of any friability in the criteria for a score of 2 was a modification to the original MES (which formally assigned 'mild friability' as a score of 1),[1] to align with current US Food and Drug Administration guidance.[2]

4. Treatment failure definition

Treatment failure was defined as an increase from OCTAVE Sustain study baseline total Mayo score of ≥3 points, with an increase in rectal bleeding subscore of ≥1 point and an increase in MES of ≥1 point yielding a MES of ≥2, after a minimum of 8 weeks of tofacitinib treatment in OCTAVE Sustain.

5. Evaluation of agreement and disagreement between the local and central endoscopy scoring methods

Agreement between central and local reads was first displayed graphically in a four-by-four table based upon the four categories of the MES. The variability amongst the 16 cells was initially evaluated by inspecting the distribution of agreement around the theoretical line of complete agreement specified by a diagonal line (e.g. a central read of 0 and local read of 0; a central read of 1 and local read of 1 etc.). In these tables, random variation in scoring should generate a distribution in the differences scattered equally on either side of the line of complete agreement, whilst a systematic variation, consistent with bias, would show a distribution skewed to one side of the line or the other.

6. Cochran-Mantel-Haenszel (CMH) chi-squared test to compare the proportion of patients in clinical remission and endoscopic response

Non-responder imputation was used for missing data, meaning that patients were treated as non-responders after the time of discontinuation up to the visit they would have reached if they had stayed in the study. No imputation for missing data was applied for patients who continued participation. The CMH chi-squared test was used to compare the proportion of patients in clinical remission and endoscopic response in the tofacitinib and placebo groups. For OCTAVE Induction 1 and 2, the CMH chi-squared test was stratified by treatment group, prior TNF antagonist treatment, corticosteroid use at induction study baseline and geographic region. For OCTAVE Sustain, the CMH chi-squared test was stratified by treatment assignment in the induction study and remission status at OCTAVE Sustain baseline.

7. References

1. Vuitton L, Peyrin-Biroulet L, Colombel JF, et al. Defining endoscopic response and remission in ulcerative colitis clinical trials: an international consensus. *Aliment Pharmacol Ther* 2017;45:801–813.

2. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER). Ulcerative colitis: clinical trial endpoints. Guidance for industry. 2016. http://www.fda.gov/downloads/Drugs/Guidances/UCM515143.pdf. Accessed July 8, 2021.

Table S1. Proportion of patients with a difference between centrally and locally read MES (two-level response) at Week 8 in OCTAVE Induction 1 and 2, Week 52 in OCTAVE Sustain and in induction non-responders at Month 2 of OCTAVE Open

	Week 8 in OCTAVE Induction 1 and 2[†] (N = 1061)			**Week 52 in OCTAVE Sustain[‡] (N = 333)**			**Month 2 in OCTAVE Open (induction non-responders)[§] (N = 382)**		
	N1	**CR ≥1 point higher or lower than LR n (%)**	**No difference between CR and LR n (%)**	**N1**	**CR ≥1 point higher or lower than LR n (%)**	**No difference between CR and LR n (%)**	**N1**	**CR ≥1 point higher or lower than LR n (%)**	**No difference between CR and LR n (%)**
Age at baseline[¶]									
<30 years	245	84 (34.3)	161 (65.7)	59	23 (39.0)	36 (61.0)	95	36 (37.9)	59 (62.1)
30 to <40 years	284	96 (33.8)	188 (66.2)	78	40 (51.3)	38 (48.7)	115	44 (38.3)	71 (61.7)
40 to <50 years	232	82 (35.3)	150 (64.7)	73	27 (37.0)	46 (63.0)	78	35 (44.9)	43 (55.1)
≥50 years	300	122 (40.7)	178 (59.3)	123	58 (47.2)	65 (52.8)	94	38 (40.4)	56 (59.6)
Sex									
Male	619	226 (36.5)	393 (63.5)	191	85 (44.5)	106 (55.5)	237	85 (35.9)	152 (64.1)
Female	442	158 (35.7)	284 (64.3)	142	63 (44.4)	79 (55.6)	145	68 (46.9)	77 (53.1)
Body mass index[¶]									
<25 kg/m^2	618	216 (35.0)	402 (65.0)	177	82 (46.3)	95 (53.7)	224	87 (38.8)	137 (61.2)
25 to <30 kg/m^2	300	123 (41.0)	177 (59.0)	107	48 (44.9)	59 (55.1)	101	38 (37.6)	63 (62.4)
≥30 kg/m^2	142	45 (31.7)	97 (68.3)	49	18 (36.7)	31 (63.3)	55	27 (49.1)	28 (50.9)

Race									
White	847	286 (33.8)	561 (66.2)	256	109 (42.6)	147 (57.4)	300	112 (37.3)	188 (62.7)
Black	8	5 (62.5)	3 (37.5)	2	0 (0.0)	2 (100.0)	4	1 (25.0)	3 (75.0)
Asian	134	61 (45.5)	73 (54.5)	50	26 (52.0)	24 (48.0)	53	30 (56.6)	23 (43.4)
Other	38	18 (47.4)	20 (52.6)	14	8 (57.1)	6 (42.9)	12	4 (33.3)	8 (66.7)
Geographic region									
North America[††]	222	89 (40.1)	133 (59.9)	62	27 (43.5)	35 (56.5)	82	35 (42.7)	47 (57.3)
Asia[‡‡]	115	55 (47.8)	60 (52.2)	43	24 (55.8)	19 (44.2)	46	28 (60.9)	18 (39.1)
Australia and New Zealand	64	27 (42.2)	37 (57.8)	14	7 (50.0)	7 (50.0)	25	13 (52.0)	12 (48.0)
Eastern Europe[§§]	307	95 (30.9)	212 (69.1)	124	46 (37.1)	78 (62.9)	92	36 (39.1)	56 (60.9)
Western Europe[¶¶]	317	102 (32.2)	215 (67.8)	77	39 (50.6)	38 (49.4)	128	38 (29.7)	90 (70.3)
Other	36	16 (44.4)	20 (55.6)	13	5 (38.5)	8 (61.5)	9	3 (33.3)	6 (66.7)
Disease duration[¶]									
<6 years	513	182 (35.5)	331 (64.5)	149	62 (41.6)	87 (58.4)	185	78 (42.2)	107 (57.8)
≥6 years	548	202 (36.9)	346 (63.1)	184	86 (46.7)	98 (53.3)	197	75 (38.1)	122 (61.9)
Extent of disease									
Proctosigmoiditis/proctitis[†††]	153	58 (37.9)	95 (62.1)	54	23 (42.6)	31 (57.4)	55	26 (47.3)	29 (52.7)
Left-sided colitis	354	140 (39.5)	214 (60.5)	106	45 (42.5)	61 (57.5)	131	47 (35.9)	84 (64.1)
Extensive colitis or pancolitis	551	186 (33.8)	365 (66.2)	171	78 (45.6)	93 (54.4)	196	80 (40.8)	116 (59.2)

Oral corticosteroid use at baseline[¶]									
Yes	491	187 (38.1)	304 (61.9)	131	55 (42.0)	76 (58.0)	154	52 (33.8)	102 (66.2)
No	570	197 (34.6)	373 (65.4)	202	93 (46.0)	109 (54.0)	228	101 (44.3)	127 (55.7)
Oral corticosteroid dose at induction study baseline									
<15 mg/day	145	53 (36.6)	92 (63.4)	49	19 (38.8)	30 (61.2)	43	16 (37.2)	27 (62.8)
≥15 mg/day	303	122 (40.3)	181 (59.7)	75	32 (42.7)	43 (57.3)	95	32 (33.7)	63 (66.3)
Other	43	12 (27.9)	31 (72.1)	12	6 (50.0)	6 (50.0)	17	5 (29.4)	12 (70.6)
None	570	197 (34.6)	373 (65.4)	197	91 (46.2)	106 (53.8)	227	100 (44.1)	127 (55.9)
Prior TNF antagonist failure at induction study baseline									
Yes	549	176 (32.1)	373 (67.9)	140	62 (44.3)	78 (55.7)	228	75 (32.9)	153 (67.1)
No	512	208 (40.6)	304 (59.4)	193	86 (44.6)	107 (55.4)	154	78 (50.6)	76 (49.4)
Prior immunosuppressant failure at induction study baseline									
Yes	770	272 (35.3)	498 (64.7)	229	99 (43.2)	130 (56.8)	293	114 (38.9)	179 (61.1)
No	291	112 (38.5)	179 (61.5)	104	49 (47.1)	55 (52.9)	89	39 (43.8)	50 (56.2)
Baseline total Mayo score[¶]									
<9	381	158 (41.5)	223 (58.5)	-	-	-	178	79 (44.4)	99 (55.6)
≥9	677	225 (33.2)	452 (66.8)	-	-	-	204	74 (36.3)	130 (63.7)
<3	-	-	-	128	55 (43.0)	73 (57.0)	-	-	-
≥3	-	-	-	205	93 (45.4)	112 (54.6)	-	-	-

Baseline partial Mayo score[¶]									
<6	255	109 (42.7)	146 (57.3)	-	-	-	150	65 (43.3)	85 (56.7)
≥6	803	274 (34.1)	529 (65.9)	-	-	-	232	88 (37.9)	144 (62.1)
<2	-	-	-	166	74 (44.6)	92 (55.4)	-	-	-
≥2	-	-	-	167	74 (44.3)	93 (55.7)	-	-	-
Partial Mayo score at assessment[‡‡‡]									
<6	774	316 (40.8)	458 (59.2)	283	136 (48.1)	147 (51.9)	292	126 (43.2)	166 (56.8)
≥6	286	68 (23.8)	218 (76.2)	7	2 (28.6)	5 (71.4)	84	24 (28.6)	60 (71.4)
CRP concentration at baseline[¶]									
<3 mg/L	381	162 (42.5)	219 (57.5)	260	120 (46.2)	140 (53.8)	156	76 (48.7)	80 (51.3)
≥3 mg/L	666	219 (32.9)	447 (67.1)	73	28 (38.4)	45 (61.6)	226	77 (34.1)	149 (65.9)
CRP concentration at assessment[§§§]									
<3 mg/L	633	270 (42.7)	363 (57.3)	225	108 (48.0)	117 (52.0)	-	-	-
≥3 mg/L	424	114 (26.9)	310 (73.1)	74	30 (40.5)	44 (59.5)	-	-	-
Number of patients randomised at site based on induction data									
<5	300	111 (37.0)	189 (63.0)	168	71 (42.3)	97 (57.7)	130	61 (46.9)	69 (53.1)
≥5	761	273 (35.9)	488 (64.1)	165	77 (46.7)	88 (53.3)	252	92 (36.5)	160 (63.5)
<10	688	254 (36.9)	434 (63.1)	242	102 (42.1)	140 (57.9)	275	115 (41.8)	160 (58.2)
≥10	373	130 (34.9)	243 (65.1)	91	46 (50.5)	45 (49.5)	107	38 (35.5)	69 (64.5)

Abbreviations: b.d., twice daily; CR, central read; CRP, C-reactive protein; LR, local read; MES, Mayo endoscopic subscore; N, number of patients in each treatment group with non-missing local and central read data; n, number of patients in each subgroup with the specified level of difference; N1, number of patients in each subgroup; TNF, tumour necrosis factor.
Proportions were based on a two-level response: no difference between central and local read; central read ≥1 point higher or lower than local read.
[†]Includes patients receiving placebo (n = 216) or tofacitinib 10 mg b.d. (n = 845).
[‡]Includes patients receiving placebo (n = 68) or tofacitinib 10 mg b.d. (n = 265).
[§]Includes patients who were non-responders after receiving tofacitinib 10 mg b.d. (n = 261) or placebo (n = 121) in OCTAVE Induction 1 or 2, all of whom received tofacitinib 10 mg b.d. in OCTAVE Open.
[¶]Baseline of OCTAVE Induction 1 or 2, OCTAVE Sustain or OCTAVE Open.
[††]Canada and the USA.
[‡‡]Japan, Korea and Taiwan.
[§§]Croatia, Czechia, Estonia, Hungary, Latvia, Poland, Romania, Russia, Serbia, Slovakia and Ukraine.
[¶¶]Austria, Belgium, Denmark, France, Germany, Israel, Italy, Netherlands, Spain and the UK.
[†††]One patient with proctitis was enrolled into OCTAVE Induction 2 as a protocol deviation and assigned to receive tofacitinib 10 mg b.d.
[‡‡‡]Week 8 for OCTAVE Induction 1 and 2, Week 52 for OCTAVE Sustain and Month 2 for OCTAVE Open Induction non-responders.
[§§§]Week 8 for OCTAVE Induction 1 and 2 and Week 52 for OCTAVE Sustain.

Table S2. Proportion of patients with a difference between centrally and locally read MES (three-level response) at Week 8 in OCTAVE Induction 1 and 2, Week 52 in OCTAVE Sustain and in induction non-responders at Month 2 of OCTAVE Open

	Week 8 in OCTAVE Induction 1 and 2[†] (N = 1061)				**Week 52 in OCTAVE Sustain[‡] (N = 333)**				**Month 2 in OCTAVE Open (induction non-responders)[§] (N = 382)**			
	N1	**CR ≥1 point lower than LR n (%)**	**No difference between CR and LR n (%)**	**CR ≥1 point higher than LR n (%)**	**N1**	**CR ≥1 point lower than LR n (%)**	**No difference between CR and LR n (%)**	**CR ≥1 point higher than LR n (%)**	**N1**	**CR ≥1 point lower than LR n (%)**	**No difference between CR and LR n (%)**	**CR ≥1 point higher than LR n (%)**
Age at baseline[¶]												
<30 years	245	29 (11.8)	161 (65.7)	55 (22.4)	59	8 (13.6)	36 (61.0)	15 (25.4)	95	11 (11.6)	59 (62.1)	25 (26.3)
30 to <40 years	284	28 (9.9)	188 (66.2)	68 (23.9)	78	9 (11.5)	38 (48.7)	31 (39.7)	115	7 (6.1)	71 (61.7)	37 (32.2)
40 to <50 years	232	14 (6.0)	150 (64.7)	68 (29.3)	73	5 (6.8)	46 (63.0)	22 (30.1)	78	3 (3.8)	43 (55.1)	32 (41.0)
≥50 years	300	26 (8.7)	178 (59.3)	96 (32.0)	123	13 (10.6)	65 (52.8)	45 (36.6)	94	6 (6.4)	56 (59.6)	32 (34.0)
Sex												
Male	619	58 (9.4)	393 (63.5)	168 (27.1)	191	26 (13.6)	106 (55.5)	59 (30.9)	237	16 (6.8)	152 (64.1)	69 (29.1)
Female	442	39 (8.8)	284 (64.3)	119 (26.9)	142	9 (6.3)	79 (55.6)	54 (38.0)	145	11 (7.6)	77 (53.1)	57 (39.3)
Body mass index[¶]												
<25 kg/m^2	618	57 (9.2)	402 (65.0)	159 (25.7)	177	17 (9.6)	95 (53.7)	65 (36.7)	224	16 (7.1)	137 (61.2)	71 (31.7)
25 to <30 kg/m^2	300	30 (10.0)	177 (59.0)	93 (31.0)	107	14 (13.1)	59 (55.1)	34 (31.8)	101	9 (8.9)	63 (62.4)	29 (28.7)
≥30 kg/m^2	142	10 (7.0)	97 (68.3)	35 (24.6)	49	4 (8.2)	31 (63.3)	14 (28.6)	55	2 (3.6)	28 (50.9)	25 (45.5)

Race												
White	847	82 (9.7)	561 (66.2)	204 (24.1)	256	26 (10.2)	147 (57.4)	83 (32.4)	300	20 (6.7)	188 (62.7)	92 (30.7)
Black	8	1 (12.5)	3 (37.5)	4 (50.0)	2	0 (0.0)	2 (100.0)	0 (0.0)	4	0 (0.0)	3 (75.0)	1 (25.0)
Asian	134	8 (6.0)	73 (54.5)	53 (39.6)	50	5 (10.0)	24 (48.0)	21 (42.0)	53	4 (7.5)	23 (43.4)	26 (49.1)
Other	38	4 (10.5)	20 (52.6)	14 (36.8)	14	3 (21.4)	6 (42.9)	5 (35.7)	12	0 (0.0)	8 (66.7)	4 (33.3)
Geographic region												
North America[††]	222	22 (9.9)	133 (59.9)	67 (30.2)	62	3 (4.8)	35 (56.5)	24 (38.7)	82	7 (8.5)	47 (57.3)	28 (34.1)
Asia[‡‡]	115	7 (6.1)	60 (52.2)	48 (41.7)	43	5 (11.6)	19 (44.2)	19 (44.2)	46	4 (8.7)	18 (39.1)	24 (52.2)
Australia and New Zealand	64	7 (10.9)	37 (57.8)	20 (31.3)	14	1 (7.1)	7 (50.0)	6 (42.9)	25	0 (0.0)	12 (48.0)	13 (52.0)
Eastern Europe[§§]	307	38 (12.4)	212 (69.1)	57 (18.6)	124	12 (9.7)	78 (62.9)	34 (27.4)	92	6 (6.5)	56 (60.9)	30 (32.6)
Western Europe[¶¶]	317	19 (6.0)	215 (67.8)	83 (26.2)	77	12 (15.6)	38 (49.4)	27 (35.1)	128	10 (7.8)	90 (70.3)	28 (21.9)
Other	36	4 (11.1)	20 (55.6)	12 (33.3)	13	2 (15.4)	8 (61.5)	3 (23.1)	9	0 (0.0)	6 (66.7)	3 (33.3)
Disease duration[¶]												
<6 years	513	58 (11.3)	331 (64.5)	124 (24.2)	149	13 (8.7)	87 (58.4)	49 (32.9)	185	16 (8.6)	107 (57.8)	62 (33.5)
≥6 years	548	39 (7.1)	346 (63.1)	163 (29.7)	184	22 (12.0)	98 (53.3)	64 (34.8)	197	11 (5.6)	122 (61.9)	64 (32.5)
Extent of disease												
Proctosigmoiditis/ proctitis[†††]	153	16 (10.5)	95 (62.1)	42 (27.5)	54	6 (11.1)	31 (57.4)	17 (31.5)	55	3 (5.5)	29 (52.7)	23 (41.8)
Left-sided colitis	354	42 (11.9)	214 (60.5)	98 (27.7)	106	13 (12.3)	61 (57.5)	32 (30.2)	131	10 (7.6)	84 (64.1)	37 (28.2)

Extensive colitis or pancolitis	551	39 (7.1)	365 (66.2)	147 (26.7)	171	16 (9.4)	93 (54.4)	62 (36.3)	196	14 (7.1)	116 (59.2)	66 (33.7)
Oral corticosteroid use at baseline[¶]												
Yes	491	52 (10.6)	304 (61.9)	135 (27.5)	131	15 (11.5)	76 (58.0)	40 (30.5)	154	8 (5.2)	102 (66.2)	44 (28.6)
No	570	45 (7.9)	373 (65.4)	152 (26.7)	202	20 (9.9)	109 (54.0)	73 (36.1)	228	19 (8.3)	127 (55.7)	82 (36.0)
Oral corticosteroid dose at induction study baseline												
<15 mg/day	145	12 (8.3)	92 (63.4)	41 (28.3)	49	6 (12.2)	30 (61.2)	13 (26.5)	43	3 (7.0)	27 (62.8)	13 (30.2)
≥15 mg/day	303	35 (11.6)	181 (59.7)	87 (28.7)	75	10 (13.3)	43 (57.3)	22 (29.3)	95	4 (4.2)	63 (66.3)	28 (29.5)
Other	43	5 (11.6)	31 (72.1)	7 (16.3)	12	0 (0.0)	6 (50.0)	6 (50.0)	17	1 (5.9)	12 (70.6)	4 (23.5)
None	570	45 (7.9)	373 (65.4)	152 (26.7)	197	19 (9.6)	106 (53.8)	72 (36.5)	227	19 (8.4)	127 (55.9)	81 (35.7)
Prior TNF antagonist failure at induction study baseline												
Yes	549	39 (7.1)	373 (67.9)	137 (25.0)	140	11 (7.9)	78 (55.7)	51 (36.4)	228	13 (5.7)	153 (67.1)	62 (27.2)
No	512	58 (11.3)	304 (59.4)	150 (29.3)	193	24 (12.4)	107 (55.4)	62 (32.1)	154	14 (9.1)	76 (49.4)	64 (41.6)
Prior immunosuppressant failure at induction study baseline												
Yes	770	69 (9.0)	498 (64.7)	203 (26.4)	229	24 (10.5)	130 (56.8)	75 (32.8)	293	24 (8.2)	179 (61.1)	90 (30.7)
No	291	28 (9.6)	179 (61.5)	84 (28.9)	104	11 (10.6)	55 (52.9)	38 (36.5)	89	3 (3.4)	50 (56.2)	36 (40.4)
Baseline total Mayo score[¶]												
<9	381	45 (11.8)	223 (58.5)	113 (29.7)	-	-	-	-	178	19 (10.7)	99 (55.6)	60 (33.7)
≥9	677	52 (7.7)	452 (66.8)	173 (25.6)	-	-	-	-	204	8 (3.9)	130 (63.7)	66 (32.4)
<3	-	-	-	-	128	15 (11.7)	73 (57.0)	40 (31.3)	-	-	-	-

≥3	-	-	-	-	205	20 (9.8)	112 (54.6)	73 (35.6)	-	-	-	-
Baseline partial Mayo score[¶]												
<6	255	31 (12.2)	146 (57.3)	78 (30.6)	-	-	-	-	150	16 (10.7)	85 (56.7)	49 (32.7)
≥6	803	66 (8.2)	529 (65.9)	208 (25.9)	-	-	-	-	232	11 (4.7)	144 (62.1)	77 (33.2)
<2	-	-	-	-	166	19 (11.4)	92 (55.4)	55 (33.1)	-	-	-	-
≥2	-	-	-	-	167	16 (9.6)	93 (55.7)	58 (34.7)	-	-	-	-
Partial Mayo score at assessment[‡‡‡]												
<6	774	74 (9.6)	458 (59.2)	242 (31.3)	283	28 (9.9)	147 (51.9)	108 (38.2)	292	21 (7.2)	166 (56.8)	105 (36.0)
≥6	286	23 (8.0)	218 (76.2)	45 (15.7)	7	1 (14.3)	5 (71.4)	1 (14.3)	84	4 (4.8)	60 (71.4)	20 (23.8)
CRP concentration at baseline[¶]												
<3 mg/L	381	51 (13.4)	219 (57.5)	111 (29.1)	260	31 (11.9)	140 (53.8)	89 (34.2)	156	14 (9.0)	80 (51.3)	62 (39.7)
≥3 mg/L	666	46 (6.9)	447 (67.1)	173 (26.0)	73	4 (5.5)	45 (61.6)	24 (32.9)	226	13 (5.8)	149 (65.9)	64 (28.3)
CRP concentration at assessment[§§§]												
<3 mg/L	633	63 (10.0)	363 (57.3)	207 (32.7)	225	24 (10.7)	117 (52.0)	84 (37.3)	-	-	-	-
≥3 mg/L	424	34 (8.0)	310 (73.1)	80 (18.9)	74	7 (9.5)	44 (59.5)	23 (31.1)	-	-	-	-
Number of patients randomised at site based on induction data												
<5	300	20 (6.7)	189 (63.0)	91 (30.3)	168	12 (7.1)	97 (57.7)	59 (35.1)	130	13 (10.0)	69 (53.1)	48 (36.9)
≥5	761	77 (10.1)	488 (64.1)	196 (25.8)	165	23 (13.9)	88 (53.3)	54 (32.7)	252	14 (5.6)	160 (63.5)	78 (31.0)
<10	688	63 (9.2)	434 (63.1)	191 (27.8)	242	23 (9.5)	140 (57.9)	79 (32.6)	275	17 (6.2)	160 (58.2)	98 (35.6)

≥10	373	34 (9.1)	243 (65.1)	96 (25.7)	91	12 (13.2)	45 (49.5)	34 (37.4)	107	10 (9.3)	69 (64.5)	28 (26.2)

Abbreviations: b.d., twice daily; CR, central read; CRP, C-reactive protein; LR, local read; N, number of patients in each treatment group with non-missing local and central read data; n, number of patients in each subgroup with the specified level of difference; N1, number of patients in each subgroup; TNF, tumour necrosis factor.

Proportions were based on a three-level response: central read ≥1 point lower than local read; no difference between central and local read; central read ≥1 point higher than local read.

[†]Includes patients receiving placebo (n = 216) or tofacitinib 10 mg b.d. (n = 845).

[‡]Includes patients receiving placebo (n = 68) or tofacitinib 10 mg b.d. (n = 265).

[§]Includes patients who were non-responders after receiving tofacitinib 10 mg b.d. (n = 261) or placebo (n = 121) in OCTAVE Induction 1 or 2, all of whom received tofacitinib 10 mg b.d. in OCTAVE Open.

[¶]Baseline of OCTAVE Induction 1 or 2, OCTAVE Sustain, or OCTAVE Open.

[††]Canada and the USA.

[‡‡]Japan, Korea and Taiwan.

[§§]Croatia, Czechia, Estonia, Hungary, Latvia, Poland, Romania, Russia, Serbia, Slovakia and Ukraine.

[¶¶]Austria, Belgium, Denmark, France, Germany, Israel, Italy, Netherlands, Spain and the UK.

[†††]One patient with proctitis was enrolled into OCTAVE Induction 2 as a protocol deviation and assigned to receive tofacitinib 10 mg b.d.

[‡‡‡]Week 8 for OCTAVE Induction 1 and 2, Week 52 for OCTAVE Sustain and Month 2 for OCTAVE Open Induction non-responders.

[§§§]Week 8 for OCTAVE Induction 1 and 2 and Week 52 for OCTAVE Sustain.